



DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2009-N-0545]

Agency Information Collection Activities; Proposed Collection; Comment Request; Biological Products: Reporting of Biological Product Deviations and Human Cells, Tissues, and Cellular and Tissue-Based Product Deviations in Manufacturing

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA, Agency, or we) is announcing an opportunity for public comment on the proposed collection of certain information by the Agency. Under the Paperwork Reduction Act of 1995 (PRA), Federal Agencies are required to publish notice in the *Federal Register* concerning each proposed collection of information, including each proposed extension of an existing collection of information, and to allow 60 days for public comment in response to the notice. This notice solicits comments on information collection requirements relating to the reporting of biological product deviations and human cells, tissues, and cellular and tissue-based product (HCT/P) deviations in manufacturing, and Forms FDA 3486 and 3486A.

DATES: Submit either electronic or written comments on the collection of information by [INSERT DATE 60 DAYS AFTER DATE OF PUBLICATION IN THE *FEDERAL REGISTER*].

ADDRESSES: You may submit comments as follows. Please note that late, untimely filed comments will not be considered. The <https://www.regulations.gov> electronic filing system will accept comments until 11:59 p.m. Eastern Time at the end of [INSERT DATE 60 DAYS AFTER DATE OF PUBLICATION IN THE *FEDERAL REGISTER*]. Comments received by

mail/hand delivery/courier (for written/paper submissions) will be considered timely if they are postmarked or the delivery service acceptance receipt is on or before that date.

Electronic Submissions

Submit electronic comments in the following way:

- Federal eRulemaking Portal: <https://www.regulations.gov>. Follow the instructions for submitting comments. Comments submitted electronically, including attachments, to <https://www.regulations.gov> will be posted to the docket unchanged. Because your comment will be made public, you are solely responsible for ensuring that your comment does not include any confidential information that you or a third party may not wish to be posted, such as medical information, your or anyone else's Social Security number, or confidential business information, such as a manufacturing process. Please note that if you include your name, contact information, or other information that identifies you in the body of your comments, that information will be posted on <https://www.regulations.gov>.
- If you want to submit a comment with confidential information that you do not wish to be made available to the public, submit the comment as a written/paper submission and in the manner detailed (see "Written/Paper Submissions" and "Instructions").

Written/Paper Submissions

Submit written/paper submissions as follows:

- Mail/Hand delivery/Courier (for written/paper submissions): Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.
- For written/paper comments submitted to the Dockets Management Staff, FDA will post your comment, as well as any attachments, except for information submitted, marked and identified, as confidential, if submitted as detailed in "Instructions."

Instructions: All submissions received must include the Docket No. FDA-2009-N-0545 for “Agency Information Collection Activities; Proposed Collection; Comment Request; Biological Products: Reporting of Biological Product Deviations and Human Cells, Tissues, and Cellular and Tissue-Based Deviations in Manufacturing; Forms FDA 3486 and 3486A.” Received comments, those filed in a timely manner (see ADDRESSES), will be placed in the docket and, except for those submitted as “Confidential Submissions,” publicly viewable at <https://www.regulations.gov> or at the Dockets Management Staff between 9 a.m. and 4 p.m., Monday through Friday, 240-402-7500.

- **Confidential Submissions**--To submit a comment with confidential information that you do not wish to be made publicly available, submit your comments only as a written/paper submission. You should submit two copies total. One copy will include the information you claim to be confidential with a heading or cover note that states “THIS DOCUMENT CONTAINS CONFIDENTIAL INFORMATION.” The Agency will review this copy, including the claimed confidential information, in its consideration of comments. The second copy, which will have the claimed confidential information redacted/blacked out, will be available for public viewing and posted on <https://www.regulations.gov>. Submit both copies to the Dockets Management Staff. If you do not wish your name and contact information to be made publicly available, you can provide this information on the cover sheet and not in the body of your comments and you must identify this information as “confidential.” Any information marked as “confidential” will not be disclosed except in accordance with 21 CFR 10.20 and other applicable disclosure law. For more information about FDA’s posting of comments to public dockets, see 80 FR 56469, September 18, 2015, or access the information at: <https://www.govinfo.gov/content/pkg/FR-2015-09-18/pdf/2015-23389.pdf>.

Docket: For access to the docket to read background documents or the electronic and written/paper comments received, go to <https://www.regulations.gov> and insert the docket

number, found in brackets in the heading of this document, into the “Search” box and follow the prompts and/or go to the Dockets Management Staff, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852, 240-402-7500.

FOR FURTHER INFORMATION CONTACT: JonnaLynn Capezzuto, Office of Operations, Food and Drug Administration, Three White Flint North, 10A-12M, 11601 Landsdown St., North Bethesda, MD 20852, 301-796-3794, PRASStaff@fda.hhs.gov.

SUPPLEMENTARY INFORMATION: Under the PRA (44 U.S.C. 3501-3521), Federal Agencies must obtain approval from the Office of Management and Budget (OMB) for each collection of information they conduct or sponsor. “Collection of information” is defined in 44 U.S.C. 3502(3) and 5 CFR 1320.3(c) and includes Agency requests or requirements that members of the public submit reports, keep records, or provide information to a third party. Section 3506(c)(2)(A) of the PRA (44 U.S.C. 3506(c)(2)(A)) requires Federal Agencies to provide a 60-day notice in the *Federal Register* concerning each proposed collection of information, including each proposed extension of an existing collection of information, before submitting the collection to OMB for approval. To comply with this requirement, FDA is publishing notice of the proposed collection of information set forth in this document.

With respect to the following collection of information, FDA invites comments on these topics: (1) whether the proposed collection of information is necessary for the proper performance of FDA’s functions, including whether the information will have practical utility; (2) the accuracy of FDA’s estimate of the burden of the proposed collection of information, including the validity of the methodology and assumptions used; (3) ways to enhance the quality, utility, and clarity of the information to be collected; and (4) ways to minimize the burden of the collection of information on respondents, including through the use of automated collection techniques, when appropriate, and other forms of information technology.

Biological Products: Reporting of Biological Product Deviations and Human Cells, Tissues, and Cellular and Tissue-Based Product Deviations in Manufacturing; Forms FDA 3486 and 3486A

Under section 351 of the Public Health Service Act (PHS Act) (42 U.S.C. 262), all biological products, including human blood and blood components, offered for sale in interstate commerce must be licensed and meet standards, including those prescribed in the FDA regulations, designed to ensure the continued safety, purity, and potency of such products. In addition, under section 361 of the PHS Act (42 U.S.C. 264), FDA may issue and enforce regulations necessary to prevent the introduction, transmission, or spread of communicable diseases between the States or possessions or from foreign countries into the States or possessions. Further, the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 351) provides that drugs and devices (including human blood and blood components) are adulterated if they do not conform with current good manufacturing practice (CGMP) assuring that they meet the requirements of the FD&C Act. Establishments manufacturing biological products, including human blood and blood components, must comply with the applicable CGMP regulations (parts 211, 606, and 820 (21 CFR parts 211, 606, and 820)) and current good tissue practice (CGTP) regulations (part 1271 (21 CFR part 1271)) as appropriate. FDA regards biological product deviation (BPD) reporting and HCT/P deviation reporting to be an essential tool in its directive to protect public health by establishing and maintaining surveillance programs that provide timely and useful information.

Section 600.14 (21 CFR 600.14), in brief, requires the manufacturer who holds the biological product license, for other than human blood and blood components, and who had control over a distributed product when the deviation occurred, to report to the Center for Biologics Evaluation and Research (CBER) or to the Center for Drug Evaluation and Research (CDER) as soon as possible but at a date not to exceed 45 calendar days after acquiring information reasonably suggesting that a reportable event has occurred. Section 606.171 (21 CFR 606.171), in brief, requires licensed manufacturers of human blood and blood components, including Source Plasma, unlicensed registered blood establishments, and transfusion services,

who had control over a distributed product when the deviation occurred, to report to CBER as soon as possible but at a date not to exceed 45 calendar days after acquiring information reasonably suggesting that a reportable event has occurred. Similarly, § 1271.350(b) (21 CFR 1271.350(b)), in brief, requires HCT/P establishments that manufacture non-reproductive HCT/Ps described in § 1271.10 (21 CFR 1271.10) to investigate and report to CBER all HCT/P deviations relating to a distributed HCT/P that relates to the core CGTP requirements, if the deviation occurred in the establishment's facility or in a facility that performed a manufacturing step for the establishment under contract, agreement or other arrangement. Form FDA 3486 is used to submit BPD reports and HCT/P deviation reports.

Respondents to this collection of information are: (1) licensed manufacturers of biological products other than human blood and blood components, (2) licensed manufacturers of blood and blood components including Source Plasma, (3) unlicensed registered blood establishments, (4) transfusion services, and (5) establishments that manufacture non-reproductive HCT/Ps regulated solely under section 361 of the PHS Act as described in § 1271.10. The number of respondents and total annual responses are based on the BPD reports and HCT/P deviation reports FDA received in fiscal year (FY) 2021. The number of licensed manufacturers and total annual responses under § 600.14 include the estimates for BPD reports submitted to both CBER and CDER. Based on the information from industry, the estimated average time to complete a deviation report is 2 hours, which includes a minimal one-time burden to create a user account for those reports submitted electronically. The availability of the standardized report form, Form FDA 3486, and the ability to submit this report electronically to CBER (CDER does not currently accept electronic filings) further streamlines the report submission process.

CBER has developed a web-based addendum to Form FDA 3486 (Form FDA 3486A) to provide additional information when a BPD report has been reviewed by FDA and evaluated as a possible recall. The additional information requested includes information not contained in the

Form FDA 3486 such as: (1) distribution pattern; (2) method of consignee notification; (3) consignee(s) of products for further manufacture; (4) additional product information; (5) updated product disposition; and (6) industry recall contacts. This information is requested by CBER through email notification to the submitter of the BPD report. This information is used by CBER for recall classification purposes. CBER estimates that 3 percent of the total BPD reports submitted to CBER would need additional information submitted in the addendum. CBER further estimates that it would take between 10 and 20 minutes to complete the addendum. For calculation purposes, CBER is using 15 minutes.

Activities such as investigating, changing standard operating procedures or processes, and follow up are currently required under parts 211 (approved under OMB control number 0910-0139), 606 (approved under OMB control number 0910-0116), 820 (approved under OMB control number 0910-0073), and 1271 (approved under OMB control number 0910-0543) and, therefore, are not included in the burden calculation for the separate requirement of submitting a deviation report to FDA.

We estimate the burden of this collection of information as follows:

Table 1.--Estimated Annual Reporting Burden¹

21 CFR Section; Activity	FDA Form Number	No. of Respondents	No. of Responses per Respondent	Total Annual Responses	Average Burden per Response	Total Hours
600.14; Reporting of product deviations by licensed manufacturers.	3486	103	6.864	707	2	1,414
606.171; Reporting of product deviations by licensed manufacturers, unlicensed registered blood establishments, and transfusion services.	3486	2,008	6.883	13,821	2	27,642
1271.350(b); HCT/P deviations	3486	80	2.575	206	2	412
Web-based Addendum	3486A ²	66	6.69	442	0.25	110.5
Total				15,176		29,578.5

¹There are no capital costs or operating and maintenance costs associated with this collection of information.

²Three percent of the number of respondents ((2,008 + 103 + 80) x 0.03 = 66) and total annual responses to CBER ((13,821 + 707 + 206) x 0.03 = 442).

Our estimated burden for the information collection reflects an overall decrease of approximately 65,014 hours and a corresponding decrease of 34,152 responses. We attribute this adjustment to a decrease in the number of deviation reports we received in FY 2021 from licensed manufacturers and unlicensed registered blood establishments under § 606.171. This is likely due to our issuance of the revised guidance document entitled “Biological Product Deviation Reporting for Blood and Plasma Establishments” (85 FR 14682, March 13, 2020), which provided blood and plasma establishments with revised recommendations related to BPD reporting. The revised guidance provided a less burdensome policy for reporting BPDs that is consistent with public health and eliminated the reporting of post donation information (PDI) events as BPD reports because these reports were no longer unexpected or unforeseeable. Given the substantial number of PDI reports FDA has received, the Agency is aware that these events occur, and the submission of additional PDI reports to FDA is unlikely to facilitate the identification of manufacturing or safety issues.

Dated: June 14, 2022.

Lauren K. Roth,

Associate Commissioner for Policy.

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